AMENDMENTS TO THE SPECIFICATION

Kindly insert the following text at page 10, line 3, of the Substitute Specification filed December 23, 2004.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a set of schematic drawings showing a general outline of seven different cyclic structures within the scope of the present invention.

FIG. 2 is a graph showing the relative G_j as a function of time before and during stimulation with Compound 2 (10^{-8} M).

FIG. 3 is a graph showing that the ability of noradrenaline (300 nM NA) to stimulate phosphoinositol turnover is considerably reduced in cultures following 10 minutes of glucose and oxygen deprivation.

FIG. 4 is a set of graphs showing that addition of Compound 2 (100 nM) had no further effect on noradrenaline (300 nM) induced increase in phosphoinositol turnover in neonatal rat cardiomyocytes during control conditions, but in cells subjected to anoxia and glucose deprivation (metabolic stress), addition of Compound 2 (100 nM) + noradrenaline (300 nM) normalized the impaired phosphoinositol turnover, an increase that was about 70% higher than the increase effected by noradrenaline alone.

FIG. 5 is a graph showing rabbit hearts perfused with either Krebs-Henseleit buffer alone (vehicle; n=11 experiments), 10^{-10} mol/l Compound 2, (n=10 experiments), or 10^{-10} mol/l of AAP10 (CE2; n=3 experiments). The increase in APD_{90} dispersion observed during hypokalemic, acute myocardial ischemia in vehicle-treated rabbit hearts was prevented by 10^{-10} mol/l of Compound 2, but not by 10^{-10} mol/l of AAP10 (CE2).

FIG. 6 is an activation map after septal stimulation is presented which failed to elicit ventricular tachycardia.

FIG. 7 is a graph showing the sustained monomorphic ventricular tachycardia (VT) induced by stimulation at the lateral epicardial ventricular pacing site caused a reentry circuit.

FIG. 8 is an activation map during epicardial activation of the first complex of the VT, which starts at -44 msec prior to the onset of the surface QRS and which corresponds to the electrogram recorded at E-C in FIG. 7.

FIG. 9 is a graph showing electrocardiographic recordings after i.v. administration of the lowest dose of Compound 2. These results demonstrate that Compound 2 effectively blocked reentry VT in this dog.

FIG. 10 is a graph showing that, after 10 minutes of incubation with 10^{-8} mol/l Compound 2, one single cell stimulated mechanically exhibited increased in intracellular calcium concentration, with a subsequent propagation of the wave, which extended to an average of 6.2 cells, a significant increase compared to before adding Compound 2 (4.5 cells).

FIG. 11 is graph showing that Compound 2 can efficiently increases gap junctional mediated intercellular calcium waves in the osteoblastic cell line ROS 17/2.8 (ROS), after incubation of the cells for 48 hours under hypoxic conditions (3-6% O_2).

FIG. 12 is a graph showing that Compound 2 is able to increase gap junctional communication and restore hypoxia-induced reductions in cellular coupling. Basic coupling under physiological conditions in ROS cells was 12 cells (n=19). After 48 hours incubation in 3-6% O_2, a reduction in dye transfer was seen to 9 cells (n=27). Compound 2 was added to the bathing solution, and the cellular coupling was restored to pre-hypoxic levels, with an average dye transfer to 12 cells (n=27).

FIG. 13 is a graph showing that Compound 2 is able to restore hypoglycemia-induced uncoupling of cells. Human osteoblastic cells were cultured in monolayers on glass coverslips and loaded with fura-2. After ATP desensitization, one single cell was stimulated mechanically, and the number of cells in the wave was recorded. Here, the wave extended to an average of 3.2 cells (n=19). Medium was changed to medium without glucose, and after 8 minutes another mechanical stimulation was performed. Now, the wave was almost blocked, with a wave propagation of only 1.4 cells (n=20). Compound 2 was added to the medium in a final concentration of 10^{-8} M. A final stimulation was performed, and now the wave was almost restored, with an average extension to 2.9 cells (n=18).

FIG. 14 is a graph showing that compound 2 increased alkaline phosphatase (ALP) activity at most of the concentrations tested, except for the highest concentration (10^{-6} mol/l), which may be toxic. To assess the effect of Compound 2 on bone formation and osteoblast activity, we measured the effect of the compound on the ALP activity of the cells. Human osteoblasts were stimulated with different concentrations of Compound 2 from $1x10^{-13}$ to $1x10^{-6}$, and compared to untreated controls.

FIG. 15 is a graph showing the effect of compound 2 on ALP activity during hypoxic conditions. Human osteoblasts were cultured for four days in 5% O_2. The medium was enriched with Compound 2 in different concentrations, and compared to the responses during normoxic conditions. During hypoxia, the Compound 2-induced stimulation of ALP activity was about 15% greater than during normoxia at all concentrations in the range 10^{-11} to 10^{-8} mol/l.